Environment International 158 (2022) 106937

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Acute and longer-term cardiovascular conditions in the Deepwater Horizon Oil Spill Coast Guard Cohort

Hristina Denic-Roberts [a,b], Nicole Rowley [c], Mark C. Haigney [d], Kate Christenbury [e], John Barrett [a], Dana L. Thomas [f], Lawrence S. Engel [g], Jennifer A. Rusiecki [a,*]

[a] Department of Preventive Medicine and Biostatistics, Uniformed Services University of the Health Sciences, Bethesda, MD, USA
[b] Oak Ridge Institute for Science and Education, MD, USA
[c] Department of Laboratory Animal Resources, Uniformed Services University of the Health Sciences, Bethesda, MD, USA
[d] Department of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD, USA
[e] Social & Scientific Systems, Inc., A DLH Holdings Corp Company ("DLH"), Durham, NC, USA
[f] United States Coast Guard Headquarters, Directorate of Health, Safety, and Work Life, Washington, D.C., USA
[g] Department of Epidemiology, Gillings School of Public Health, University of North Carolina, Chapel Hill, NC, USA

ARTICLE INFO

Handling Editor: Zorana Jovanovic Andersen

Keywords:
Oil Spill
Deepwater Horizon
Cardiovascular health
Responder
Crude oil
Dispersants

ABSTRACT

Introduction: In 2010, the U.S. Coast Guard (USCG) led a clean-up response to the Deepwater Horizon (DWH) oil spill. Human studies evaluating acute and longer-term cardiovascular conditions associated with oil spill-related exposures are sparse. Thus, we aimed to investigate prevalent and incident cardiovascular symptoms/conditions in the DHW Oil Spill Coast Guard Cohort.

Methods: Self-reported oil spill exposures and cardiovascular symptoms were ascertained from post-deployment surveys (n = 4,885). For all active-duty cohort members (n = 45,193), prospective cardiovascular outcomes were classified via International Classification of Diseases, 9th Edition from military health encounter records up to 5.5 years post-DWH. We used log-binomial regression to calculate adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) in the cross-sectional analyses and Cox Proportional Hazards regression to calculate adjusted hazard ratios (aHR) and 95% CIs for incident cardiovascular diagnoses during 2010–2015 and stratifying by earlier (2010–2012) and later (2013–2015) time periods.

Results: Prevalence of *chest pain* was associated with increasing levels of crude oil exposure via inhalation ($aPR_{high\ vs.\ none}$ = 2.00, 95% CI = 1.16–3.42, p-trend = 0.03) and direct skin contact ($aPR_{high\ vs.\ none}$ = 2.72, 95% CI = 1.30–5.16, p-trend = 0.03). Similar associations were observed for *sudden heartbeat changes* and for being in the vicinity of burning oil exposure. In prospective analyses, responders (vs. non-responders) had an elevated risk for *mitral valve disorders* during 2013–2015 (aHR = 2.12, 95% CI = 1.15–3.90). Responders reporting ever (vs. never) crude oil inhalation exposure were at increased risk for *essential hypertension*, particularly *benign essential hypertension* during 2010–2012 (aHR = 2.00, 95% CI = 1.08–3.69). Responders with crude oil inhalation exposure also had an elevated risk for *palpitations* during 2013–2015 (aHR = 2.54, 95% CI = 1.36–4.74). Cardiovascular symptoms/conditions aPR and aHR estimates were generally stronger among responders reporting exposure to both crude oil and oil dispersants than among those reporting neither.

Conclusions: In this large study of the DWH oil spill USCG responders, self-reported spill clean-up exposures were associated with acute and longer-term cardiovascular symptoms/conditions.

Abbreviations: aHR, Adjusted hazard ratio; aPR, Adjusted prevalence ratio; CHD, Coronary heart disease; CI, Confidence interval; CVD, Cardiovascular disease; DOSS, Dioctyl sodium sulfosuccinate; DWH, Deepwater Horizon; DWH-CG Cohort, DWH Oil Spill Coast Guard Cohort; GuLF Study, the Gulf Long Term Follow-up Study; HEROS Study, the Health Effects Research of Oil Spill Study; ICD-9, the International Classification of Diseases, 9th Revision; MDR, the Military Health System Data Repository; MI, Myocardial infarction; OEI, Oil exposure index; OMSEP, Occupational Medical Surveillance and Evaluation Program; PAHs, Polycyclic aromatic hydrocarbons; USCG, the U.S. Coast Guard; VOCs, Volatile organic compounds.

* Corresponding author at: 4301 Jones Bridge Road, Room E-2009, Bethesda, MD 20814, USA.
E-mail address: jennifer.rusiecki@usuhs.edu (J.A. Rusiecki).

https://doi.org/10.1016/j.envint.2021.106937
Received 19 April 2021; Received in revised form 25 August 2021; Accepted 11 October 2021
Available online 20 October 2021

1. Introduction

The *Deepwater Horizon* (DWH) disaster was the largest marine oil spill in U.S. history. After a catastrophic explosion on the offshore drilling rig off Louisiana's coast on April 20, 2010, 185 to 210 million gallons of crude oil were discharged from a deep sea riser into the Gulf of Mexico until July 15, 2010, when the well was effectively capped (Federal On Scene Coordinator, 2011; Graham et al., 2011; Berenshtein et al., 2020; McNutt et al., 2012; Crone and Tolstoy, 2010). Additionally, around two million gallons of the chemical oil dispersants Corexit™ 9500 and 9527A were applied mainly below the water surface and aerially, in an effort to disperse the spilled oil (Federal On Scene Coordinator, 2011). The U.S. Coast Guard (USCG) led the national interagency clean-up response with nearly 8,700 responders. The USCG responders, along with thousands of other clean-up workers and Gulf residents, were potentially exposed to a complex mixture of harmful crude oil constituents such as volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons (PAHs), and heavy metals, as well as particulate matter, oil dispersants, and high ambient heat. These exposures may have adversely affected the health of the DWH clean-up workers.

Although oil spill disasters continue to occur worldwide, the adverse health effects among exposed response workers, particularly long-term health effects, are largely unknown. To date, human health studies assessing oil spill consequences of clean-up workers have largely been cross-sectional, focusing on acute physical and mental health symptoms (Aguilera et al., 2010; Laffon et al., 2016). While most frequently reported acute physical symptoms among oil spill-exposed workers have been respiratory in nature (e.g., runny nose, cough, sore throat, wheezing) (Alexander et al., 2018; Carrasco et al., 2006; Meo et al., 2008; Na et al., 2012; Peres et al., 2016; Suarez et al., 2005), several studies have also reported acute neurological symptoms (e.g., headaches, lightheadedness) (Carrasco et al., 2006; Na et al., 2012; Cheong et al., 2011; Ha et al., 2012; Krishnamurthy et al., 2019), dermal irritation (Na et al., 2012; Cheong et al., 2011; Baars, 2002), and fatigue (Cheong et al., 2011; Ha et al., 2012). A few cross-sectional studies of general physiological symptoms among oil spill clean-up workers or residents of affected communities have also reported acute cardiovascular symptoms such as chest pain and tightness, sudden heartbeat changes, and palpitations (Cheong et al., 2011; Ha et al., 2012; Campbell et al., 1993; Meo et al., 2009; Rusiecki et al., 2017).

Given that crude oil constituents can affect the cardiovascular system via various mechanisms (Abplanalp et al., 2017; Marris et al., 2020), it is biologically plausible that exposure to crude oil may have adverse effects on cardiovascular health. For instance, inhalation of particulate matter containing PAHs has been associated with cardiovascular morbidity and mortality in animals and humans through mechanisms of cardiotoxicity, atherosclerosis, cardiac arrhythmias, and cardiac hypertrophy (Marris et al., 2020). The use of oil dispersants and surface burning can interact with and change the structure of PAHs, further increasing their potential toxicity (Millemann et al., 2015). A crude oil constituent, benzene, has also been associated with increased markers for cardiovascular disease in mice and humans (Abplanalp et al., 2017). Several recent studies of fish affected by the DWH oil spill have linked exposure to weathered DWH crude oil samples to adverse cardiovascular effects such as dose-dependent defects in cardiac function, pericardial edema, irregular atrial arrhythmia, disrupted regulation of cellular excitability, reduced myocyte contractility, and reduced stroke volume and cardiac output (Brette et al., 2014; Esbaugh et al., 2016; Incardona et al., 2014; Nelson et al., 2016; Heuer et al., 2019). Additionally, two studies of rats exposed to Corexit™ 9500 via inhalation demonstrated a transient, but not longer-term, increase in heart rate and blood pressure (Krajnak et al., 2011; Roberts et al., 2014). Dioctyl sodium sulfosuccinate (DOSS), a component of Corexit™ 9500 used in the DWH clean-up, may also act as an obesogen (Temkin et al., 2016; Bowers et al., 2016) and, therefore, pose as a cardiovascular risk factor.

The few prospective studies of long-term health effects associated with oil spill exposures have focused primarily on longer-term respiratory effects (Gam et al., 2018a; Gam et al., 2018b; Lawrence et al., 2020; Noh et al., 2019; Zock et al., 2014; Zock et al., 2007). Cardiovascular health effects among oil spill clean-up workers have been investigated in only two prospective cohorts to date (Strelitz et al., 2018; Strelitz et al., 2019a; Strelitz et al., 2019b; Lee et al., 2020). In the Gulf Long Term Follow-up (GuLF) Study, longer duration of working on the DWH spill (>180 days vs. 1-30 days) and stopping work because of heat were each significantly associated with a two-fold increased risk of self-reported myocardial infarction (MI) up to three years post-spill (Strelitz et al., 2018). In the same cohort, after five years of follow-up, longer duration of working on the DWH spill remained associated with increased hazard of self-reported MI or fatal coronary heart disease (CHD), although the association was attenuated (HR = 1.43, 95% CI: 0.91–2.25) (Strelitz et al., 2019a). After five years of follow-up, the GuLF Study investigators also found that living in proximity of the DWH spill (vs. away from the spill) (Strelitz et al., 2019) and having a higher estimated exposure to total hydrocarbons (≥3.00 ppm vs. < 0.30 ppm) (Strelitz et al., 2019) were each significantly associated with increased hazards of self-reported MI/fatal CHD (HR = 1.30, 95% CI: 1.01–1.67 and 1.81, 1.11–2.95, respectively). In the Health Effects Research of Oil Spill (HEROS) study, clean-up workers were followed up to 10 years after the Hebei Spirit oil spill off the coast of South Korea (Lee et al., 2020). In this study, Lee and colleagues found that longer duration of working on the spill (180+ days vs. 0–14 days) was associated with an increased hazard of self-reported newly diagnosed angina or MI (HR = 2.06, 95% CI: 1.05–4.03).

Because understanding of both acute and longer-term human cardiovascular health effects associated with exposure to crude oil and/or oil dispersants is very limited, but biologically plausible, we aimed to investigate these associations among USCG DWH responders in the large (N = 53,519), prospective DWH Oil Spill Coast Guard (DWH-CG) Cohort (Rusiecki et al., 2017). In the present study, we evaluated both prevalent and incident cardiovascular symptoms and conditions associated with the DWH oil spill response. Our objective was to assess risks associated with the response itself, as well as with self-reported exposures to crude oil and to combined crude oil and oil dispersant, up through five and a half years following the spill using self-reported post-deployment survey data as well as objective health encounter data from the equal-access Military Health System.

2. Materials and methods

2.1. Study population and study design

The DWH-CG Cohort has been previously described in detail (Rusiecki et al., 2017). The cohort was established with an aim of studying both acute symptoms and longer-term health conditions associated with the DWH oil spill response. The study, therefore, consists of two components, one cross-sectional and one prospective. Briefly, 53,519 USCG members (8,696 members who responded to the DWH oil spill, "responders," and 44,823 members who did not respond to the DWH oil spill, "non-responders") who were either on active duty or in the Selected Reserve between the start of the oil spill (20 April 2010) and the beginning of the transitional phase of the oil spill response (Federal On Scene Coordinator, 2011) (17 December 2010) were identified via USCG administrative databases and included in the cohort study. For the cross-sectional component of the current analysis, we included 4,885 responders (either active duty or Select Reservists) who completed a post-deployment survey that elicited information on both the oil spill exposures and cardiovascular symptoms during deployment. For the prospective component of the current analysis, we included only active duty responders (N = 5,964) and non-responders (N = 39,260) because only the active duty military personnel (and not the Select Reservists) have comprehensive medical coverage through the equal-access Military Health System and, thus,

ongoing health encounter data available for measuring cardiovascular disease (CVD) diagnoses.

This study was approved by the Institutional Review Boards of the Uniformed Services University, the U.S. Coast Guard, and the University of North Carolina, Chapel Hill.

2.2. Exposure assessment

Self-reported information on exposure to crude oil/oily water (hereafter referred to as "crude oil") and oil dispersant (hereafter referred to as "dispersant") was derived from two post-deployment surveys completed by the USCG responders (N = 5,665 total; n = 3,492 active duty). These surveys have been previously described (Rusiecki et al., 2017). Briefly, Survey 1 was administered beginning in June of 2010 and Survey 2 beginning in November of 2010. Although the two surveys queried similar information, Survey 1 assessed self-reported exposures to crude oil via different routes - inhalation, skin contact, ingestion, and submersion - on a binary "never/ever" scale, while Survey 2 evaluated these exposures on a 5-point Likert scale ("never," "rarely," "sometimes," "most of the time," and "all of the time"). Self-reported exposures to being in the *vicinity* of crude oil or being in contact with dispersants were ascertained only in Survey 2, also on a 5-point Likert scale.

For the cross-sectional component of the current analysis (N = 4,885), we utilized the following self-reported exposure metrics from Survey 2: 1) inhalation of crude oil vapors (low: "rarely" or "sometimes", and high: "most of the time" or "all of the time" vs. none: "never"); 2) direct skin contact with crude oil (low, high vs. none); 3) being in the vicinity of burning oil (ever: "rarely," "sometimes," "most of the time," or "all of the time" vs. "never"); and 4) combined crude oil and dispersant exposures. For the combined crude oil/dispersant exposure metric, we created the following exposure groups: "no oil/no dispersant" (i.e., reporting "never" being exposed to crude oil via any route *and* reporting "never" or "rarely" being exposed to dispersant); "oil only" (i.e., reporting "ever" being exposed to crude oil via any route *but* "never" or "rarely" being exposed to dispersant); and "oil and dispersant" (i.e., reporting "ever" being exposed to crude oil via any route *and* being exposed to dispersant "sometimes," "most of the time," or "all of the time"). In this analysis the "no oil/no dispersant" group was the referent.

For the prospective analyses, restricted to active duty responders and non-responders, we conducted three primary comparisons: 1) responder vs. non-responder, for which the exposure was participation in any type of DWH oil spill response work, 2) within-responder comparisons in relation to crude oil exposure via inhalation, and 3) within-responder comparisons in relation to combined crude oil/dispersant exposure which incorporated crude oil exposure via any route. For the crude oil inhalation comparisons, we used self-reported exposure data from both post-deployment surveys and created the following exposure metric: ever ("ever" from Survey 1 and "sometimes," "most of the time," or "all of the time" from Survey 2) vs. never ("never" from Survey 1 and "never" or "rarely" from Survey 2). We used the same combined crude oil/dispersant exposure metric for the prospective analyses as for the cross-sectional analyses, comparing "oil only" and "oil and dispersant" to "no oil/no dispersant".

2.3. Outcome assessment

For the cross-sectional analyses, acute cardiovascular symptoms were ascertained from Survey 2. The following two questions were asked using a 3-point Likert scale ("never," "sometimes," "most of the time"): 1) "During deployment, did you experience Chest Pain?", and 2) "During deployment, did you experience Sudden Heartbeat Changes?" The two separate outcomes of *chest pain* and *sudden heartbeat changes* were treated as binary on a never/ever scale by collapsing responses of "sometimes" and "most of the time" into an "ever" category.

For the prospective analyses, we ascertained cardiovascular outcomes using medical health encounter data maintained by the military in a large data repository, the Military Health System Data Repository (MDR), which has been described previously (Rusiecki et al., 2017; Rhon et al., 2018). Briefly, the MDR contains data of inpatient and outpatient health encounters obtained from both military treatment facilities/clinics ("direct care") and non-military treatment facilities (i.e., civilian) for which care is billed to the military ("purchased care"). For all active duty cohort members, we obtained medical encounter data from the MDR for a period between 01 October 2007 and 30 September 2015 by combining four major data sources consisting of inpatient and outpatient direct/military care and inpatient and outpatient purchased/civilian care. We therefore had data coverage for approximately two and a half years prior to the DWH spill and approximately five and a half years post-spill. Health encounter MDR data for the dates we queried were coded using the International Classification of Diseases, 9th Revision (ICD-9). In this study, we focused on chronic cardiovascular diseases and symptoms classified by three-, four-, or five-digit ICD-9 codes. We considered ICD-9 codes for *Diseases of the Circulatory System* (ICD-9: 390–459), *Symptoms involving cardiovascular system* (ICD-9: 785) and *Chest pain* (ICD-9: 786.5), which is found under the *Symptoms involving respiratory system and other chest symptoms* (ICD-9: 786) category. A full listing of diseases and symptoms that we evaluated and their corresponding ICD-9 codes is provided in Table A.1 in the supplement. The case definition we used required at least one inpatient encounter or two outpatient encounters for a specific cardiovascular disease or symptom. To avoid data sparsity issues, we retained only outcomes with at least 10 cases per exposure group, guided by the largest overall sample size in the responder vs. non-responder comparison.

2.4. Statistical analyses

2.4.1. Cross-sectional analyses

We used log-binomial regression to model cross-sectional associations between oil spill exposures and self-reported prevalence of *chest pain* and *sudden heartbeat changes* by calculating adjusted prevalence ratios (aPR) and 95% confidence intervals (95% CI) (Deddens and Petersen, 2008). In the event of non-convergence of the log-binomial models, we used the COPY method (SAS macro) with 1,000,000 copies (Petersen and Deddens, 2009). We adjusted each model for confounders selected *a priori,* guided by directed acyclic graphs (Greenland et al., 1999; Shrier and Platt, 2008). All crude oil exposures (crude oil inhalation, direct skin contact with crude oil, and being in the vicinity of burning oil) and the crude oil/dispersant combination exposure were adjusted for age (years), smoking status (never; former; current), deployment timing (pre-capping: started and ended deployment prior to well capping; *peri*-capping: started pre- and ended post-well capping; post-capping: started and ended post-well capping), sleep deprivation (<6 h sleep and 30+ days deployment; all other sleep/deployment duration combinations), and self-reported exhaust inhalation exposure (none; low; high). We also considered adjusting for ambient heat (estimated mean daily heat index), however, the associations were not significantly affected by this covariate (PRs changed < 10%) and we, therefore, did not include ambient heat in the final models. To assess exposure–response associations, we conducted tests for linear trend by modeling exposures with more than two levels (none/low/high for crude oil inhalation and direct skin contact) as pseudo-continuous variables.

2.4.1.1. Cross-sectional sensitivity analyses. To assess the robustness of the cross-sectional associations and to account for potential influence of pre-existing cardiovascular conditions, we performed a sensitivity analysis excluding those responders with pre-existing medical diagnoses related to *chest pain* and *sudden heartbeat changes* (arrhythmias) utilizing the pre-DWH spill MDR data from 01 October 2007 to 20 April 2010. Because complete health encounter MDR data were available only for active duty cohort members, this sensitivity analysis was limited to

active duty personnel (n = 3,102). We queried ICD-9 codes to identify conditions related to chest pain and arrhythmias and provided a full list of exclusion conditions in Table A.2 in the supplement. The case definition used for exclusion was having either one inpatient or two outpatient health encounters for the selected condition any time between 01 October 2007 and the responder's start date of DWH deployment in 2010.

2.4.2. Prospective analyses

We limited all prospective analyses to medically deployable active duty responders and non-responders. We excluded 31 USCG members (one responder and 30 non-responders) with evidence from a centralized USCG database of personnel not meeting deployment readiness requirements in the time period immediately prior to the DWH oil spill.

To examine associations between the crude oil and oil/dispersant exposure metrics described above and the risk of cardiovascular diseases/symptoms, we performed multivariable Cox Proportional Hazards regression analyses yielding adjusted hazard ratios (aHRs) and 95% CIs. We included ICD-9 codes in any diagnostic position for our main analyses. The start of follow-up time for all active duty cohort members was the later of 20 April 2010 or the entry date into the USCG. The end of follow-up was the earliest of 1) the date of becoming a case of a particular cardiovascular condition, 2) the end of follow-up period (30 September 2015), or 3) the USCG exit date. Prevalent cases among the responders and non-responders, who had a cardiovascular disease/symptom before the spill (01 October 2007–20 April 2010) ascertained via the same case definition as a post-DWH case, were excluded from all analyses of that particular cardiovascular outcome.

Our main analyses for the within-responder exposure comparisons (ever/never crude oil via inhalation and crude oil/dispersant comparisons) were adjusted for age at baseline (years), sex (male; female), race (white; Black; other/unknown) and smoking status (never; former; current; unknown). The responder vs. non-responder models were adjusted only for age, sex, and race because smoking information was not available for non-responders or for responders without survey data.

We tested the proportionality of hazards assumption across the five and a half year follow-up period (20 April 2010 – 30 September 2015) by evaluating Pearson correlations between Schoenfeld residuals and follow-up time. A p-value for the corresponding Pearson correlation coefficient of <0.05 suggested non-proportionality of hazards. In those cases where the assumption was violated, we calculated adjusted HRs and 95% CIs for two approximately equal-length time periods, i.e., 20 April 2010 – 31 December 2012 (the "earlier period") and 01 January 2013 – 30 September 2015 (the "later period").

2.4.2.1. Prospective sensitivity analyses. We performed three sensitivity analyses. First, we refined our case definition by restricting the relevant ICD-9 codes to either the first or the second diagnostic position (instead of *any* diagnostic position). Because this restriction greatly reduced the number of cardiovascular cases, we limited this sensitivity analysis to the comparison of responders to non-responders. Second, for both responder vs. non-responder and within-responder analyses, we excluded cohort members who were under more intensive periodic medical surveillance through enrollment in the Coast Guard's Occupational Medical Surveillance and Evaluation Program (OMSEP) at the time of the DWH oil spill or during the follow-up period. Certain USCG occupations with a high probability for occupational exposure to known or suspected toxins (e.g., benzene exposure) require enrollment in the OMSEP and are followed more closely through baseline and periodic physical examinations in accordance with the Occupational Safety and Health Administration requirements (U.S. Coast Guard, 2018). Because cohort members enrolled in the OMSEP were already a high-risk group due to their prior occupational exposures, we believed that they could be at an even higher risk for developing chronic disease after participating in the DWH clean-up, and thus, might bias our risk estimates for cardiovascular diseases/symptoms. Lastly, because tobacco smoke contains some of the same constituents as crude oil (i.e., benzene, PAHs, heavy metals) and has a strong association with cardiovascular disease (Fowles and Dybing, 2003), for our final sensitivity analysis, we restricted the within-responder comparisons for the ever/never crude oil exposure via inhalation to those responders who reported never smoking. This restriction to never smokers allowed us to rule out any potential residual confounding by smoking.

All cross-sectional and prospective analyses were performed in SAS Version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Baseline cohort characteristics

Table 1 depicts baseline characteristics of three groups studied here: 1) active duty non-responders (n = 39,230) included in the prospective analyses, 2) active duty responders with post-deployment survey data (n = 3,491) included in the prospective analyses, and 3) responders included in the cross-sectional analyses consisting of both active duty (64%) and Selected Reserve (36%) members with Survey 2 data (n = 4,855). The mean baseline age among active duty cohort members was 30 years, while the responder group included in the cross-sectional analysis was slightly older (mean age 33 years). All three groups were predominantly male (~85%) and white (~77%). Smoking information was available only for responders. Over half (54%) of active duty responders reported never smoking, 15% were former smokers, 22.5% were current smokers, while the smoking status of the remaining 8.5% was unknown. A greater proportion of the responders included in the cross-sectional analysis were never smokers (65.1%) and former smokers (16.2%), while the remaining 18.7% reported currently smoking.

Table 1
Baseline characteristics of the Deepwater Horizon Oil Spill Coast Guard Cohort.

Characteristic	Active duty non-responders * (N = 39,230)	Active duty responders with survey data* (N = 3,491)	Responders with Survey 2 data for cross-sectional analyses (N = 4,855)
Age (years)			
Mean (SD)	30.3 (8.2)	30.9 (7.6)	33.1 (8.6)
Median (IQR)	28 (24–36)	30 (25–36)	32 (26–29)
Age category, n (%)			
<25 years	11,323 (28.9%)	767 (22.0%)	827 (17.0%)
25–34 years	17,056 (43.5%)	1,716 (49.1%)	2,128 (43.8%)
35–50 years	10,295 (26.2%)	968 (27.7%)	1,738 (35.8%)
>50 years	556 (1.4%)	40 (1.2%)	162 (3.4%)
Sex, n (%)			
Male	33,512 (85.4%)	3,028 (86.7%)	4,127 (85.0%)
Female	5,718 (14.6%)	463 (13.3%)	728 (15.0%)
Race, n (%)			
White	30,185 (76.9%)	2,702 (77.4%)	3,741 (77.0%)
Black	2,181 (5.6%)	167 (4.9%)	203 (4.2%)
Other/ unknown	6,864 (17.5%)	622 (17.7%)	911 (18.8%)
Employee class, n (%)			
Active duty	39,230 (100%)	3,491 (100%)	3,102 (63.9%)
Select Reserve	0 (0%)	0 (0%)	1,753 (36.1%)
Smoking status, n (%)			
Never	–	1,887 (54.0%)	3,159 (65.1%)
Former	–	521 (15.0%)	788 (16.2%)
Current	–	786 (22.5%)	908 (18.7%)
Unknown	–	297 (8.5%)	0 (0%)

* Used in prospective analyses.

3.2. Cross-sectional findings

Table 2 summarizes cross-sectional associations between self-reported crude oil and crude oil/dispersant exposures and acute cardiovascular symptoms among the 4,855 responders with Survey 2 data. Increasing levels of crude oil exposure via inhalation ($aPR_{high\ vs.\ none}$ = 2.00, 95% CI: 1.16–3.42, p-trend = 0.03) and direct skin contact ($aPR_{high\ vs.\ none}$ = 2.72, 95% CI: 1.30–5.16, p-trend = 0.03) were associated with reports of *chest pain*. A report of ever vs. never being in the vicinity of burning oil was also associated with increased *chest pain* prevalence (aPR = 2.30, 95% CI: 1.52–3.44). Compared to responders reporting neither being exposed to crude oil nor dispersant, those with exposure to both had a suggestive elevation of prevalence of *chest pain* (aPR = 1.49, 95% CI: 0.76–2.80), while those exposed to oil only did not (aPR = 0.81, 95% CI: 0.52–1.28). Similarly, increasing levels of crude oil exposure via inhalation ($aPR_{high\ vs.\ none}$ = 2.68, 95% CI: 1.42–5.06, p-trend = 0.003), direct skin contact ($aPR_{high\ vs.\ none}$ = 2.74, 95% CI: 1.19–5.56, p-trend = 0.06), and ever (vs. never) exposure to being in the vicinity of burning oil (aPR = 1.76, 95% CI: 1.10–2.75) were associated with elevated prevalence of *sudden heartbeat changes*. Self-reported exposure to both crude oil and oil dispersant (vs. exposure to neither) was associated with *sudden heartbeat changes* (aPR = 2.43, 95% CI: 1.12–5.06), while the association with the exposure to "oil only" (vs. exposure to neither) was lower in magnitude (aPR = 1.48, 95% CI: 0.89–2.57).

The cross-sectional sensitivity analyses among active duty responders with Survey 2 data (n = 3,102) and among active duty responders without pre-existing diagnoses related to chest pain (n = 2,998) and arrhythmias (n = 3,035) are presented in Table A.3 in the supplement. Compared to the main associations among both active duty and Selected Reserve responders with Survey 2 data (n = 4,855, Table 2), the associations between all self-reported exposures and both acute cardiovascular outcomes among active-duty responders were slightly stronger and followed the same patterns. The magnitude and patterns of associations remained stable after exclusion of pre-existing diagnoses related to both chest pain and arrhythmias.

3.3. Prospective findings

3.3.1. Responder vs. non-responder comparisons

The adjusted hazard ratios (aHRs) for incident cardiovascular diseases/symptoms post-DWH oil spill, comparing all active duty responders (n = 5,963) to non-responders (n = 39,230), adjusted for age, sex, and race, are presented in Table 3. The proportionality of hazards assumption over the five-year follow-up period (2010–2015) was violated for one of the outcomes (*mitral valve disorders*), as evidenced by a Schoenfeld residual p-value of 0.03. Therefore, we conducted the analyses for this particular outcome separately in the earlier (2010–2012) and later time period (2013–2015) (Table 3 footnote). The risk for m*itral valve disorders* was elevated in responders compared to non-responders in the later time period (aHR = 2.12, 95% CI: 1.15–3.90), but not in the earlier time period (aHR = 0.83, 95% CI: 0.42–1.67). In the overall follow-up period, we found elevated risks for *other forms of chronic ischemic heart disease* (aHR = 1.27), *coronary atherosclerosis* (aHR = 1.18), *other diseases of endocardium* (aHR = 1.14), and *atrial fibrillation and flutter* (aHR = 1.26), and reduced risks for *cardiac dysrhythmias* (aHR = 0.87), *premature beats* (aHR = 0.83), and *undiagnosed cardiac murmurs* (aHR = 0.87) among the responders, however, these associations were not statistically significant.

In the sensitivity analyses where we restricted cardiovascular cases to those with the ICD-9 codes in either the first or the second diagnostic position, we observed similar patterns and magnitudes of associations for most of the outcomes (Table A.4 in the supplement), despite the number of cardiovascular cases being substantially reduced.

After exclusion of 2,257 (6.4%) non-responders and 638 (10.7%) responders enrolled in OMSEP during the follow-up period (Table A.5 in the supplement), the general patterns of risk remained similar to the main analysis, although some of the effects were attenuated. The proportionality of hazards assumption over the five-year follow-up period was not violated for any of the outcomes.

3.3.2. Within-responder comparisons

For all of the within-responder comparisons, we present a smaller number of cardiovascular diseases/symptoms for which there were at least 10 events per exposure group in the overall follow-up period

Table 2
Cross-sectional associations between self-reported oil spill exposures and acute cardiovascular symptoms among DWH USCG responders (N = 4,855).

	Chest pain (n = 108)				Sudden heartbeat changes (n = 96)			
Self-reported exposure	N	PR[1]	(95% CI)	p-trend	N	PR[1]	(95% CI)	p-trend
Crude oil inhalation								
None	39	1.00	–		27	1.00	–	
Low[2]	40	0.78	(0.49–1.25)		46	1.40	(0.84–2.41)	
High[3]	29	2.00	(1.16–3.42)	0.03	23	2.68	(1.42–5.06)	0.003
Direct skin contact with crude oil								
None	53	1.00	–		48	1.00	–	
Low[2]	45	1.21	(0.80–1.83)		40	1.16	(0.74–1.80)	
High[3]	10	2.72	(1.30–5.16)	0.03	8	2.74	(1.19–5.56)	0.06
Being in the vicinity of burning oil								
Never	71	1.00	–		69	1.00	–	0.01
Ever	37	2.30	(1.52–3.44)	–	27	1.76	(1.10–2.75)	–
Crude oil/oil dispersant[4]								
No oil/no dispersant[5]	37	1.00	–		24	1.00	–	
Oil only[6]	57	0.81	(0.52–1.28)	0.14	60	1.48	(0.89–2.57)	0.14
Oil & Dispersant[7]	14	1.49	(0.76–2.80)	–	12	2.43	(1.12–5.06)	–

[1] Adjusted for age (years), smoking (never, former, current), deployment timing (pre-/peri-capping, post-capping), sleep deprivation (<6 hrs sleep/30 + days deployment vs. everyone else), and exhaust exposure (none, low, high).
[2] Combines Survey 2 responses of "rarely" and "sometimes".
[3] Combines Survey 2 responses of "most of the time" and "all of the time".
[4] Six responders who reported being exposed to oil dispersant "sometimes", "most of the time" or "all of the time", but "never" being exposed to crude oil are missing from the oil/dispersant combination analyses.
[5] "No oil/no dispersant" exposure combines "Never" exposure to crude oil via any route and "Never" or "Rarely" exposure to dispersant from Survey 2.
[6] "Oil only" exposure combines "Ever" exposure to crude oil via any route and "Never" or "Rarely" exposure to dispersant from Survey 2.
[7] "Oil & Dispersant" exposure combines "Ever" exposure to crude oil via any route and "Sometimes", "Most of the time" and "All of the time" exposure to dispersant from Survey 2.

Table 3
Risk of cardiovascular conditions comparing active duty DWH USCG responders to non-responders; MDR data 2010–2015, ICD-9 diagnostic codes in any position.

	Responder (N = 5,963)		Non-responder (N = 39,230)			
Condition (ICD-9 code)	**N**	**Person Years**	**N**	**Person Years**	**HR[1] (95% CI)**	**Schoenfeld p-value[2]**
Essential hypertension (401)	329	24,649	2,121	164,642	1.02 (0.90–1.14)	0.44
Benign essential hypertension (401.1)	104	26,080	678	174,491	1.06 (0.86–1.31)	0.79
Unspecified essential hypertension (401.9)	303	24,818	2,083	165,473	0.96 (0.85–1.08)	0.26
Other forms of chronic ischemic heart disease (414)	25	26,506	130	177,165	1.27 (0.82–1.95)	0.52
Coronary atherosclerosis (414.0)	22	26,511	123	177,202	1.18 (0.75–1.86)	0.72
Other diseases of endocardium (424)	31	26,453	186	176,882	1.14 (0.77–1.67)	0.28
Mitral valve disorders (424.0)	23	26,493	121	177,160	1.32 (0.84–2.07)	**0.03***
Conduction disorders (426)	24	26,458	164	176,929	0.95 (0.62–1.46)	0.96
Cardiac dysrhythmias (427)	93	26,125	710	174,781	0.87 (0.70–1.08)	0.47
Atrial fibrillation and flutter (427.3)	20	26,517	105	177,241	1.26 (0.78–2.04)	0.30
Premature beats (427.6)	25	26,468	194	177,023	0.83 (0.54–1.26)	0.23
Other venous embolism and thrombosis (453)	21	26,506	136	177,220	1.02 (0.64–1.61)	0.69
Symptoms involving cardiovascular system (785)	255	25,429	1,681	170,124	1.03 (0.90–1.17)	0.76
Tachycardia, unspecified (785.0)	35	26,475	240	176,864	0.97 (0.68–1.38)	0.11
Palpitations (785.1)	143	25,974	889	174,045	1.06 (0.89–1.26)	0.88
Undiagnosed cardiac murmurs (785.2)	29	26,447	235	176,549	0.87 (0.59–1.28)	0.80
Chest pain (786.5)	338	24,794	2,378	166,556	0.96 (0.85–1.07)	0.96

[1] All models adjusted for age (years), sex (male, female), and race (White, Black, Other/Unknown).
[2] Schoenfeld p-value for proportionality of hazards.
* Because of the proportionality of hazards assumption violation for *mitral valve disorders* during 2010–2015, we evaluated results by two equal sub-periods and results were: 2010–2012: $N_{responders} = 9$, $N_{non\text{-}responders} = 82$, HR = 0.83, 95% CI: 0.42–1.67 and 2013–2015: $N_{responders} = 14$, $N_{non\text{-}responders} = 39$, HR 2.12, 95% CI: 1.15–3.90.

(2010–2015), or at least 8 events per exposure group in the two separate time periods (2010–2012 or 2013–2015).

Table 4 shows age-, sex-, race-, and smoking-adjusted HRs, comparing active duty responders who reported ever exposure to crude oil via inhalation to responders reporting never exposure. In the overall follow-up period, where the proportionality assumption was not violated, there were non-statistically significant elevated risks for *essential hypertension* (aHR = 1.23, 95% CI: 0.92–1.64) and its subcategory *unspecified essential hypertension* (aHR = 1.16, 95% CI: 0.85–1.57), as well as for *chest pain* (aHR = 1.29, 95% CI: 0.96–1.74). For the rest of the cardiovascular outcomes, we performed period-specific analyses, given the Schoenfeld p-values < 0.05. The risk for *benign essential hypertension* was elevated in the earlier period (aHR = 2.00, 95% CI: 1.08–3.69), but we did not have sufficient number of cases in the later period to meaningfully evaluate this association. In contrast, the risks for developing *symptoms involving cardiovascular system* and its subcategory *palpitations* were elevated in the later (aHR = 2.26, 95% CI: 1.37–3.71 and aHR = 2.54, 95% CI: 1.36–4.74, respectively), but not in the earlier time period (aHRs = 0.88, 95% CI: 0.56–1.36 and aHR = 0.71, 95% CI: 0.37–1.37, respectively). A similar pattern of elevated risk in the later time period was observed for *cardiac dysrhythmias* (aHR = 1.68, 95% CI: 0.80–3.56), however, the low number of events in the earlier time period precluded us from being able to interpret the HR.

In the sensitivity analysis excluding 407 (11.7%) responders enrolled in OMSEP during the follow-up period (Table A.6 in the supplement), patterns of risk remained similar to the main analysis presented in Table 4. In another sensitivity analysis, restricted to the 54% of responders who reported never smoking (Table A.7 in the supplement), the risk for developing *essential hypertension* over the five-year follow-up period slightly increased (aHR = 1.55, 95% CI: 1.02–2.36). The risks for developing *symptoms involving cardiovascular system* and its subcategory *palpitations* in the later time period (aHR = 2.67, 95 %CI: 1.39–5.13 and aHR = 4.14, 95 %CI: 1.72–9.93, respectively) also increased, although the precision of the estimates decreased due to the lower number of cases in these sensitivity analyses.

The associations of self-reported exposure to both crude oil and dispersant ("Oil & Dispersant") compared to neither exposure are presented in Table 5. For comparative purposes, we present these results alongside associations for the exposure to crude oil without dispersant ("Oil only") versus exposure to neither. Because the proportionality of hazards assumption was violated for *essential hypertension* and its subcategory *unspecified essential hypertension*, as well as for *symptoms involving cardiovascular system* and its subcategory *palpitations*, we performed period-specific analyses for these four outcomes. *Essential hypertension* risk was significantly elevated in the earlier time period for the "Oil only" vs. neither comparison (aHR = 1.75, 95% CI: 1.13–2.72)

Table 4
Risk of cardiovascular conditions among active duty DWH USCG responders reporting ever[1] (N = 1,068) vs. never[2] (N = 2,423) exposure to crude oil via inhalation; MDR data 2010–2015, ICD-9 diagnostic codes in any position.

	2010–2015				2010–2012			2013–2015		
Condition (ICD-9 code)	**N[3]**	**N[4]**	**HR[5] (95% CI)**	**Schoenfeld p-value[6]**	**N[3]**	**N[4]**	**HR[5] (95% CI**	**N[3]**	**N[4]**	**HR[5] (95% CI)**
Essential hypertension (401)	72	153	1.23 (0.92–1.64)	0.20			–			
Benign essential hypertension (401.1)	24	47	1.48 (0.89–2.47)	0.049	18	30	2.00 (1.08–3.69)	6	17	–
Unspecified essential hypertension (401.9)	64	145	1.16 (0.85–1.57)	0.42			–			
Cardiac dysrhythmias (427)	18	38	1.09 (0.62–1.94)	0.04	5	23	–	13	15	1.68 (0.80–3.56)
Symptoms involving cardiovascular system (785)	60	108	1.30 (0.94–1.79)	0.01	28	76	0.88 (0.56–1.36)	32	32	2.26 (1.37–3.71)
Palpitations (785.1)	34	60	1.32 (0.86–2.03)	<0.01	12	41	0.71 (0.37–1.37)	22	19	2.54 (1.36–4.74)
Chest pain (786.5)	68	141	1.29 (0.96–1.74)	0.56			–			

[1] Ever included those reporting "Ever" on Survey 1 or "Sometimes," "Most of the Time," or "All of the Time" on Survey 2.
[2] Never included those reporting "Never" on Survey 1 or "Never" or "Rarely" on Survey 2.
[3] Number of cases for a given condition among responders exposed to crude oil via inhalation.
[4] Number of cases for a given condition among responders not exposed to crude oil via inhalation.
[5] All models adjusted for age (years), sex (male, female), race (White, Black, Other/Unknown), and smoking (never, former, current, unknown).
[6] Schoenfeld p-value for proportionality of hazards.

Table 5
Risk of cardiovascular conditions among active duty DWH USCG responders reporting exposure to crude oil, but no oil dispersant (N = 1,351) or crude oil and oil dispersant (N = 448) vs. neither exposure (N = 1,282); MDR data 2010–2015, ICD-9 diagnostic codes in any position.

	2010–2015		2010–2012		2013–2015	
Condition (ICD-9 code)	**N**	**HR[1] (95% CI)**	**N**	**HR[1] (95% CI)**	**N**	**HR[1] (95% CI)**
Essential hypertension (401)[2]						
No oil/no dispersant[3]	76	1.00	43	1.00	33	1.00
Oil only[4]	83	1.26 (0.91–1.75)	53	1.75 (1.13–2.72)	30	0.81 (0.49–1.34)
Oil & Dispersant[5]	35	1.45 (0.96–2.20)	23	1.91 (1.11–3.26)	12	0.99 (0.50–1.93)
Benign essential hypertension (401.1)						
No oil/no dispersant[3]	30	1.00				
Oil only[4]	26	1.03 (0.59–1.79)		–		–
Oil & Dispersant[5]	7	0.78 (0.33–1.82)				
Unspecified essential hypertension (401.9)[2]						
No oil/no dispersant[3]	70	1.00	41	1.00	29	1.00
Oil only[4]	77	1.27 (0.90–1.78)	48	1.66 (1.05–2.60)	29	0.89 (0.53–1.49)
Oil & Dispersant[5]	33	1.47 (0.95–2.25)	21	1.82 (1.04–3.17)	12	1.08 (0.54–2.14)
Cardiac dysrhythmias (427)						
No oil/no dispersant[3]	21	1.00				
Oil only[4]	23	1.19 (0.65–2.19)		–		–
Oil & Dispersant[5]	8	1.19 (0.51–2.75)				
Symptoms involving cardiovascular system (785)[2]						
No oil/no dispersant[3]	61	1.00	43	1.00	18	1.00
Oil only[4]	65	1.09 (0.76–1.55)	40	0.96 (0.62–1.49)	25	1.33 (0.72–2.45)
Oil & Dispersant[5]	29	1.40 (0.90–2.20)	12	0.83 (0.43–1.58)	17	2.76 (1.41–5.42)
Palpitations (785.1)[2]						
No oil/no dispersant[3]	32	1.00	21	1.00	11	1.00
Oil only[4]	35	1.10 (0.68–1.80)	20	1.01 (0.54–1.88)	15	1.27 (0.58–2.78)
Oil & Dispersant[5]	19	1.68 (0.95–3.00)	7	1.00 (0.42–2.39)	12	2.87 (1.26–6.57)
Chest pain (786.5)						
No oil/no dispersant[3]	70	1.00				
Oil only[4]	73	1.10 (0.79–1.54)		–		–
Oil & Dispersant[5]	30	1.46 (0.94–2.27)				

[1] All models adjusted for age (years), sex (male, female), race (White, Black, Other/Unknown), and smoking (never, former, current, unknown).
[2] Violated the proportionality of hazards assumption based on Schoenfeld p-value < 0.05.
[3] "No oil/no dispersant" exposure combines "Never" exposure to crude oil via any route and "Never" or "Rarely" exposure to dispersant from Survey 2.
[4] "Oil only" exposure combines "Ever" exposure to crude oil via any route and "Never" or "Rarely" exposure to dispersant from Survey 2.
[5] "Oil & Dispersant" exposure combines "Ever" exposure to crude oil via any route and "Sometimes", "Most of the time" and "All of the time" exposure to dispersant from Survey 2.

and even more strongly elevated for the combined "Oil & Dispersant" (vs. neither) comparison (aHR = 1.91, 95% CI: 1.11–3.26), but the estimates were null in the later time period. We observed a similar pattern for *unspecified essential hypertension* in the earlier time period ("Oil only" aHR = 1.66, 95% CI: 1.05–2.60 and "Oil & Dispersant" aHR = 1.82, 95% CI: 1.04–3.17). In contrast, the risk for *symptoms involving cardiovascular system* was elevated in the later, but not in the earlier, time period for the "Oil only" exposure (aHR = 1.33, 95% CI: 0.72–2.45) and more strongly for the "Oil & Dispersant" exposure (aHR = 2.76, 95% CI: 1.41–5.42). We observed a similar pattern for *palpitations* in the later time period ("Oil only" aHR = 1.27, 95% CI: 0.58–2.78 and "Oil & Dispersant" aHR = 2.87, 95% CI: 1.26–6.57). In the overall time period (2010–2015), where the proportionality assumption was not violated, the combined crude oil/dispersant exposure was associated with slightly elevated risk of *chest pain* (aHR = 1.46, 95% CI: 0.94–2.27), while the association for the "Oil only" exposure was null (aHR = 1.10, 95% CI: 0.79–1.54).

4. Discussion

In this study of young, generally healthy U.S. Coast Guard service members, we found that self-reported exposures to crude oil and to combined crude oil and dispersants were associated with increased prevalence of *chest pain* and *sudden heartbeat changes* during the *Deepwater Horizon* oil spill response. These cross-sectional associations strengthened in sensitivity analyses upon exclusion of responders with pre-spill medical diagnoses related to chest pain and arrhythmias. In prospective analyses, including active duty USCG members with continuous military healthcare coverage, we found evidence of increased risks for diagnoses of certain cardiovascular diseases and symptoms during five and a half years of follow-up post-DWH spill. Compared to non-responders, responders had a two-fold increased risk for *mitral valve disorders* diagnosis during the second half of follow-up (2013–2015). Compared to non-exposed responders, those who reported being exposed to crude oil via inhalation were at increased risk for *essential hypertension* diagnosis, particularly during the first half of follow-up (2010–2012). Responders who reported crude oil inhalation were also at a two-fold increased risk of being diagnosed with *symptoms involving cardiovascular system*, including *palpitations*, during the second half of follow-up. Risk estimates for *essential hypertension* and *palpitations* were slightly stronger for responders reporting exposure to both crude oil and oil dispersants compared to those reporting neither. The patterns of prospective associations remained robust across a range of sensitivity analyses.

Our cross-sectional findings of significant associations between self-reported oil spill exposures and increased prevalence of acute *chest pain* and *sudden heartbeat changes* are in agreement with prior literature (Cheong et al., 2011; Ha et al., 2012; Campbell et al., 1993; Meo et al., 2009; Rusiecki et al., 2017). Two previous studies of self-reported acute health symptoms in the wake of the 1993 Braer spill near the coast of the Shetland Islands, Scotland (Campbell et al., 1993) and the 2003 *Tasman Spirit* oil spill near Karachi, Pakistan (Meo et al., 2009) reported elevated odds of chest ache/tightness. In the Braer oil spill investigation, the exposed residents reported elevated symptoms of chest ache after the spill in comparison to their experience of chest aches prior to the spill (OR = 3.20, 95% CI: 1.28–8.01) (Campbell et al., 1993). When the exposed residents were compared to a non-exposed, control community, the odds of reporting chest ache symptoms attenuated (unadjusted OR = 1.39, 95% CI: 0.44–4.90). In a small study in the wake of the *Tasman Spirit* oil spill (Meo et al., 2009), apparently healthy, non-smoking male clean-up workers had increased odds of reporting chest tightness compared to similar, matched controls (unadjusted OR = 9.77, 95% CI:

0.52–186.7). Although these two studies assessed crude oil exposure rather crudely (i.e., living in the vicinity of the spill and participating in the spill clean-up) and did not account for any potential confounding factors in their analyses, our findings of elevated prevalence of self-reported chest pain with increasing levels of crude oil exposure provide further evidence for this association. In a previous analysis of our study population (Rusiecki et al., 2017), we did not find evidence of increased prevalence of *chest pain* in association with an oil exposure index that combined participants' response duration, period of response, and self-reported crude oil exposure. However, in the current analysis, we focused on more comprehensive metrics of crude oil exposure (via inhalation, direct skin contact, and being in the vicinity of burning oil) and did observe significant associations with self-reported acute *chest pain*. The finding of elevated acute *chest pain* was consistent with results of our prospective analysis comparing responders who reported crude oil inhalation exposure to non-exposed responders (Table 4), which found a slightly elevated risk of the *chest pain* symptom during the five year study follow-up (aHR = 1.29, 95% CI: 0.96–1.74).

In previous investigations of acute health symptoms after the 2007 *Hebei Spirit* oil spill (Cheong et al., 2011; Ha et al., 2012), longer duration of participating in the spill clean-up was associated with elevated odds of reporting palpitations (adjusted $OR_{20+\text{ vs. }10\text{-}12\text{ days}} = 8.55$, 95% CI: 1.89–38.62) (Cheong et al., 2011). While our study assessed *sudden heartbeat changes*, a non-specific symptom which may be interpreted as a sudden increase in heart rate, a flutter, or a skipped beat (i.e., palpitations), or as a sudden decrease in heart rate, we believe that this acute symptom is likely to be interpreted by most responders as palpitations. In our previous publication (Rusiecki et al., 2017), we found a suggestive association between increasing levels of the oil exposure index (OEI) and prevalence of *sudden heartbeat changes* ($aPR_{\text{OEI high vs. none}} = 1.50$, 95% CI: 0.85–2.66, p-trend = 0.17). This association was stronger in our current analysis in which we used more comprehensive crude oil exposure metrics. Our findings, therefore, corroborate those from the *Hebei Spirit* oil spill (Ha et al., 2012) and our previous investigation (Rusiecki et al., 2017). To our knowledge, this study is the first to report a higher prevalence of acute cardiovascular symptoms in relation to combined crude oil and dispersant exposure than to crude oil exposure alone.

Four other analyses from two prospective cohorts have investigated longer-term cardiovascular outcomes among oil spill clean-up workers (Strelitz et al., 2018; Strelitz et al., 2019a; Strelitz et al., 2019b; Lee et al., 2020). After five years of follow-up in the GuLF Study, longer duration of participating in the DWH spill clean-up (aHR = 1.43, 95% CI: 0.91–2.25) (Strelitz et al., 2019a), living in the proximity of the spill (aHR = 1.30, 95%CI: 1.01–1.67) (Strelitz et al., 2019a), and higher estimated exposure to total hydrocarbons (aHR = 1.81, 95% CI: 1.11–2.95) (Strelitz et al., 2019b) were associated with increased risk of self-reported MI or fatal CHD. In our prospective analyses of the USCG responders to the DWH spill, we did not have a sufficient number of health encounters to evaluate risk of acute MI diagnosis and we lacked data on fatal CHD, but we did observe non-statistically significant elevated risks for *other forms of chronic ischemic heart disease* (aHR = 1.27, 95% CI: 0.82–1.95) and its subcategory, *coronary atherosclerosis* (aHR = 1.18, 95% CI: 0.75–1.86) in responder vs. non-responder comparisons (Table 3). These estimates were robust in sensitivity analyses in which we restricted the ICD-9 codes to the first or second diagnostic position and also when we excluded cohort members who were enrolled in the Coast Guard's occupational medical surveillance program OMSEP during the study follow-up. Because our study population was young (mean age 30 years) and healthy at baseline, we did not expect to observe severe heart disease such as MI or CHD after only five and a half years of follow-up. In contrast to our study population, approximately 60% of the GuLF Study participants were 40 years of age or older and not likely to be as healthy as active duty military service members, thus, our populations are not directly comparable with respect to developing chronic heart disease. Nevertheless, in our within-responder analyses, we did consistently observe an elevated risk of *essential hypertension*, which is a major risk factor for developing CHD, and which we discuss in more detail below (Fuchs and Whelton, 2020). Similarly to the GuLF Study, the HEROS study, which followed the *Hebei Spirit* oil spill clean-up workers for up to 10 years post-spill (Lee et al., 2020), observed an increased risk of self-reported incident angina or MI (aHR = 2.06, 95% CI: 1.05–4.03) with longer duration of spill clean-up. Not only was the HEROS' study follow-up twice as long as ours, but the mean age of their study participants at baseline was twice the age of our study population, or 60 years, so comparisons with the present study should be made with caution.

In the responder vs. non-responder analysis, we observed a two-fold increased risk for *mitral valve disorders* diagnosis during the second half of follow-up (2013–2015). This finding, based on a relatively small number of health encounters, could have been a statistical anomaly and should be interpreted with caution and further investigated in other studies. A low number of encounters for *mitral valve disorders* in the within-responder analyses precluded us from further examining this association. Because irregular heart beat can be one of the symptoms of mitral valve disease, it is possible that our finding of a two-fold increased risk of *palpitations*, also during the second half of follow-up, among the responders exposed to crude oil via inhalation is a marker for undiagnosed disease involving the mitral valve. As previous fish studies have indicated, exposure to PAHs via weathered DWH crude oil samples was associated with cardiac arrhythmias through cardiotoxic mechanisms such as disrupted excitation–contraction coupling in cardiomyocytes (Brette et al., 2014; Incardona et al., 2014). Air pollution studies also provide evidence that inhaling particulate matter containing PAHs is associated with cardiac arrhythmias (Marris et al., 2020; Brook et al., 2010). Although palpitations are not specific to cardiac arrhythmias, our finding of increased palpitations is mechanistically plausible. Additionally, we did evaluate *cardiac dysrhythmias* as a separate outcome and despite the low number of health encounters, we observed that responders exposed to crude oil via inhalation had a modestly elevated risk during the second half of the study follow-up (aHR = 1.68, 95% CI 0.80–3.56).

As mentioned above, in our within-responder analyses, those who reported being exposed to crude oil via inhalation were at increased risk for *essential hypertension* diagnosis, particularly its subcategory *benign essential hypertension* during the first half of follow-up. This association persisted even among never smokers, indicating a mechanism other than smoking. Although, to our knowledge, there have not been any other oil spill studies evaluating this association, living in an oil- and gas-polluted area was associated with increased prevalence of hypertension in a recent cross-sectional study in Nigeria (Ezejimofor et al., 2016). A limited number of human studies also provide evidence that air pollution may play a role in hypertension via mechanisms of inflammation and oxidative stress (Brook et al., 2010; Mannucci et al., 2019). In our study, risk estimates for *essential hypertension* were slightly stronger for responders reporting exposure to both crude oil and dispersants compared to those reporting neither, during the first half, but not the second half of follow-up. To our knowledge, the only similar evidence comes from two laboratory studies demonstrating that male Sprague-Dawley rats acutely exposed to Corexit™ 9500A (i.e., oil dispersant used in the DWH clean-up response) via inhalation had a transient, but not longer-term, increase in heart rate and blood pressure compared to non-exposed controls (Krajnak et al., 2011; Roberts et al., 2014).

Our study has several strengths. We investigated acute and longer-term cardiovascular symptoms/conditions associated with combined crude oil and dispersants exposure, shedding light on the impact of this realistic exposure scenario on human health. We also utilized several important metrics of exposure to crude oil by evaluating different routes of exposure such as inhalation, skin contact, and burning oil. Our sample size was large, which allowed us to assess the robustness of our main findings through various sensitivity analyses. To our knowledge, our study was the first to ascertain longer-term cardiovascular outcomes from an objective, comprehensive database of health encounters, thereby reducing the potential for recall errors in disease ascertainment. The access to universal military healthcare coverage of this population

also reduced the potential for selection bias or differential loss to follow-up. Since our study population consisted of generally young and healthy active duty military service members, the likelihood of existing co-morbidities was low. Because we had health encounter data prior to the spill, we were able to additionally exclude any pre-existing cardiovascular diagnoses from both the cross-sectional and prospective analyses. For part of our prospective analyses, we ascertained health encounter data for a reference group of USCG members who were medically deployable but did not participate in the DWH spill clean-up; this enabled us to compare the DWH responders to a similar group of non-responders. However, although we excluded 31 non-medically ready service members from the prospective analyses, it is likely that there were considerably more cohort members than we could identify who were not fit for deployment due to different reasons, such as injury, pregnancy, not meeting weight standards, or awaiting medical clearance for various conditions. Because at the time of the DWH oil spill the USCG did not have a comprehensive, centralized database of personnel not fit for deployment, our study utilized the only database available at that time. The U.S. military recently estimated that over 10% of military service members are not fit for deployment (Shane, 2019) and the USCG estimates are similar (personal communication with Dana L. Thomas on March 14, 2021).

Our study findings should be interpreted considering several potential limitations. Primarily, our exposure metrics relied on self-report and we did not have any individual-level occupational monitoring data for our cohort members. While self-reported exposure responses may have been influenced by recall errors, the exit surveys were administered relatively shortly after deployment and we believe any error is likely to be nondifferential; the median time between end of deployment and survey completion was one day for Survey 1 and 153 days for Survey 2 (Rusiecki et al., 2017). A lack of data on potentially confounding factors not routinely recorded in the MDR, such as body mass index, cholesterol levels, diet, and physical activity, limited our ability to perform further statistical adjustments, although we do not expect that these unmeasured factors differed by exposure status. Because our population was young and healthy, the follow-up time of up to five and half years post-spill was not long enough for most to develop "hard" cardiovascular events, such as MI, which typically take a long time to develop. Most of our analyses were therefore limited to evaluating relatively non-specific outcomes such as *symptoms involving cardiovascular system*, including *palpitations*. However, some of these symptoms may pose as risk factors for, or precursors to, more severe CVD in the future, as our cohort ages. While we used objective health encounter data to define cardiovascular outcomes, it is important to note that ICD coding may be susceptible to classification inaccuracies such as variations in electronic medical records across different facilities and coder errors (O'Malley et al., 2005). Nevertheless, ICD coding is widely used in epidemiological research (O'Malley et al., 2005) and military surveillance (O'Donnell et al., 2018) because it is generally a reliable indicator of disease and symptoms diagnoses when interpreted appropriately. For our prospective case definitions, we used two outpatient visits or one inpatient visit in order to increase the diagnostic accuracy of ICD-9 code classifications. We also performed sensitivity analyses limiting ICD-9 codes to the first or second diagnostic position. One of our future efforts will be utilizing procedure codes and pharmacy data to further refine case definitions. We conducted multiple comparisons using various exposure metrics and outcomes which could have resulted in observing statistically significant results by chance. However, given the novelty of assessing longer-term health impacts of oil spill exposures, we attempted to evaluate patterns of association rather than test specific hypotheses. It is also important to note that because our population was predominantly white and male, and relatively young and healthy, the generalizability of our findings to other oil spill populations is limited. Considering the above-mentioned limitation of a long latency period for developing heart disease and our relatively young and healthy study population, one of our future investigations will evaluate whether DWH exposures are associated with cardiovascular disease risk factors such as obesity, dyslipidemia, and sleep disturbances.

4.1. Conclusions

In conclusion, in this large study of U.S. Coast Guard responders to the *Deepwater Horizon* oil spill, we found evidence of positive associations between oil spill clean-up exposures and both acute and longer-term cardiovascular symptoms/conditions. Given the limited knowledge of long-term health consequences of oil spills, the frequency and volume of oil spill disasters, the recent relaxation of offshore drilling regulations (Federal Register, 2017), and the aggressive expansion of deepwater drilling (National Commission, 2011), even in remote areas, it is of essential public health importance to continue to study long-term health consequences of oil spill exposures. Our study findings could help mitigate adverse health outcomes in future disaster response efforts.

Funding

This work was supported by the National Institutes of Health (grant RO1ES020874). One of the authors (HDR) was supported by an appointment to the Department of Defense (DOD) Research Participation Program administered by the Oak Ridge Institute for Science and Education (ORISE) through an interagency agreement between the U.S. Department of Energy (DOE) and the DOD. ORISE is managed by ORAU under DOE contract number DE-SC0014664.

Disclaimer

All opinions expressed here are the authors' and do not necessarily reflect the policies and official views of the Uniformed Services University of the Health Sciences, the Department of Defense, the United States Coast Guard, the Department of Homeland Security, the Oak Ridge Institute for Science and Education, or the Department of Energy.

Disclosures

The authors have no disclosures to report.

Data Statement

Since these data are from military data resources based on military personnel health encounters, the process for obtaining assurances for public use would involve authorizations, not only by the Department of Defense but also by the U.S. Coast Guard. These data could be made available to others in the private and public sector, given all appropriate agreements covering such transfer could be executed. This would have to be managed on a case-by-case basis.

CRediT authorship contribution statement

Hristina Denic-Roberts: Conceptualization, Methodology, Formal analysis, Writing – original draft. **Nicole Rowley:** Formal analysis, Writing – review & editing. **Mark C. Haigney:** Writing – review & editing. **Kate Christenbury:** Formal analysis, Writing – review & editing. **John Barrett:** Writing – review & editing. **Dana L. Thomas:** Writing – review & editing. **Lawrence S. Engel:** Conceptualization, Methodology, Writing – review & editing. **Jennifer A. Rusiecki:** Conceptualization, Methodology, Investigation, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors would like to thank the US Coast Guard for providing data for this study and Dr. David Jackson, formerly at U.S. Army Center for Environmental Health Research, for organizing ORISE support for the study.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2021.106937.

References

Abplanalp, W., DeJarnett, N., Riggs, D.W., et al., 2017. Benzene exposure is associated with cardiovascular disease risk. PLoS ONE 12 (9), e0183602. https://doi.org/10.1371/journal.pone.0183602 [published Online First: 2017/09/09].

Aguilera, F.M.J., Pasaro, E., Laffon, B., 2010. Review on the effects of exposure to spilled oils on human health. J. Appl. Toxicol. 30, 291–301.

Alexander, M., Engel, L.S., Olaiya, N., et al., 2018. The deepwater horizon oil spill coast guard cohort study: A cross-sectional study of acute respiratory health symptoms. Environ Res 162, 196–202. https://doi.org/10.1016/j.envres.2017.11.044.

Baars, B., 2002. The wreckage of the oil tanker 'Erika'–human health risk assement of beach cleaning, sunbathing and swimming. Toxicol. Lett. 128, 55–68.

Berenshtein, I., Paris, C.B., Perlin, N., et al., 2020. Invisible oil beyond the Deepwater Horizon satellite footprint. Sci. Adv. 6 (7), eaaw886. https://doi.org/10.1126/sciadv.aaw8863 [published Online First: 2020/02/26].

Bowers, R.R., Temkin, A.M., Guillette, L.J., et al., 2016. The commonly used nonionic surfactant Span 80 has RXRalpha transactivation activity, which likely increases the obesogenic potential of oil dispersants and food emulsifiers. Gen. Comp. Endocrinol. 238, 61–68. https://doi.org/10.1016/j.ygcen.2016.04.029 [published Online First: 2016/05/02].

Brette, F., Machado, B., Cros, C., et al., 2014. Crude oil impairs cardiac excitation-contraction coupling in fish. Science 343 (6172), 772–776. https://doi.org/10.1126/science.1242747.

Brook, R.D., Rajagopalan, S., Pope 3rd, C.A., et al., 2010. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation 121 (21), 2331–2378. https://doi.org/10.1161/CIR.0b013e3181dbece1 [published Online First: 2010/05/12].

Campbell, D.C.D., Crum, J., Foster, K., Christie, P., Brewster, D., 1993. Initial effects of the grounding of the tanker Braer on health in Shetland. BMJ 307, 1251–1255.

Carrasco, J., Lope, V., Perez-Gomez, B., et al., 2006. Association between health information, use of protective devices and occurrence of acute health problems in the Prestige oil spill clean-up in Asturias and Cantabria (Spain): a cross-sectional study. BMC Public Health 6, 1.

Cheong, H.K., Ha, M., Lee, J.S., et al., 2011. Hebei spirit oil spill exposure and subjective symptoms in residents participating in clean-up activities. Environ. Health Toxicol. 26, e2011007. https://doi.org/10.5620/eht.2011.26.e2011007 [published Online First: 2011/11/30].

Crone, T.J., Tolstoy, M., 2010. Magnitude of the 2010 Gulf of Mexico oil leak. Science 330 (6004), 634. https://doi.org/10.1126/science.1195840 [published Online First: 2010/10/12].

Deddens, J.A., Petersen, M.R., 2008. Approaches for estimating prevalence ratios. Occup. Environ. Med. 65 (7), 481501–481506. https://doi.org/10.1136/oem.2007.034777 [published Online First: 2008/06/20].

Esbaugh, A.J., Mager, E.M., Stieglitz, J.D., et al., 2016. The effects of weathering and chemical dispersion on Deepwater Horizon crude oil toxicity to mahi-mahi (Coryphaena hippurus) early life stages. Sci. Total Environ. 543 (Pt A), 644–651. https://doi.org/10.1016/j.scitotenv.2015.11.068 [published Online First: 2015/11/28].

Ezejimofor, M.C., Uthman, O.A., Maduka, O., et al., 2016. The Burden of Hypertension in an Oil- and Gas-Polluted Environment: A Comparative Cross-Sectional Study. Am. J. Hypertens. 29 (8), 925–933. https://doi.org/10.1093/ajh/hpw009 [published Online First: 2016/02/18].

Federal On Scene Coordinator, 2011. On Scene Coordinator Report: Deewpater Horizon Oil Spill.

Federal Register, 2017. Oil and Gas and Sulphur Operations on the Outer Continental Shelf—Oil and Gas Production Safety Systems—Revisions Bureau of Safety and Environmental Enforcement, Department of the Interior, 61703-61724.

Fowles, J., Dybing, E., 2003. Application of toxicological risk assessment principles to the chemical constituents of cigarette smoke. Tob Control 12 (4), 424–430. https://doi.org/10.1136/tc.12.4.424 [published Online First: 2003/12/09].

Fuchs, F.D., Whelton, P.K., 2020. High Blood Pressure and Cardiovascular Disease. Hypertension 75 (2), 285–292. https://doi.org/10.1161/HYPERTENSIONAHA.119.14240 [published Online First: 2019/12/24].

Gam, K.B., Kwok, R.K., Engel, L.S., et al., 2018. Exposure to Oil Spill Chemicals and Lung Function in Deepwater Horizon Disaster Response Workers. J. Occup. Environ. Med. 60 (6), e312–e318. https://doi.org/10.1097/JOM.0000000000001292 [published Online First: 2018/02/02].

Gam, K.B., Kwok, R.K., Engel, L.S., et al., 2018. Lung Function in Oil Spill Response Workers 1–3 Years After the Deepwater Horizon Disaster. Epidemiology 29 (3), 315–322. https://doi.org/10.1097/EDE.0000000000000808 [published Online First: 2018/01/31].

Graham, B.R.W., Beinecke, F., Boesch, D., Garcia, T., Murray, C., Ulmer, F., 2011. Deep water: The gulf oil disaster and the future of offshore drilling. National Commission on the BP Deepwater Horizon Oil Spill and Offshore Drilling.

Greenland, S., Pearl, J., Robins, J.M., 1999. Causal diagrams for epidemiologic research. Epidemiology 10 (1), 37–48 [published Online First: 1999/01/15].

Ha, M., Kwon, H., Cheong, H.K., et al., 2012. Urinary metabolites before and after cleanup and subjective symptoms in volunteer participants in cleanup of the Hebei Spirit oil spill. Sci. Total Environ. 429, 167–173. https://doi.org/10.1016/j.scitotenv.2012.04.036. Epub 12 May 15.

Heuer, R.M., Galli, G.L.J., Shiels, H.A., et al., 2019. Impacts of Deepwater Horizon Crude Oil on Mahi-Mahi (Coryphaena hippurus) Heart Cell Function. Environ. Sci. Technol. 53 (16), 9895–9904. https://doi.org/10.1021/acs.est.9b03798 [published Online First: 2019/07/26].

Incardona, J.P., Gardner, L.D., Linbo, T.L., et al., 2014. Deepwater Horizon crude oil impacts the developing hearts of large predatory pelagic fish. Proc. Natl. Acad. Sci. U S A 111 (15), E1510–E1518 doi: 10.073/pnas.1320950111 Epub 2014 Mar 24.

Krajnak, K., Kan, H., Waugh, S., et al., 2011. Acute effects of COREXIT EC9500A on cardiovascular functions in rats. J. Toxicol. Environ. Health A 74 (21), 1397–1404. https://doi.org/10.1080/15287394.2011.606795 [published Online First: 2011/09/16].

Krishnamurthy, J., Engel, L.S., Wang, L., et al., 2019. Neurological symptoms associated with oil spill response exposures: Results from the Deepwater Horizon Oil Spill Coast Guard Cohort Study. Environ. Int. 131, 104963. https://doi.org/10.1016/j.envint.2019.104963 [published Online First: 2019/08/06].

Laffon, B., Pasaro, E., Valdiglesias, V., 2016. Effects of exposure to oil spills on human health: Updated review. J. Toxicol. Environ. Health B Crit. Rev. 19 (3–4), 105–128. https://doi.org/10.1080/10937404.2016.1168730. Epub 2016 May 24.

Lawrence, K.G., Keil, A.P., Garantziotis, S., et al., 2020. Lung function in oil spill responders 4–6 years after the Deepwater Horizon disaster. J Toxicol Environ Health A 83 (6), 233–248. https://doi.org/10.1080/15287394.2020.1745111 [published Online First: 2020/04/07].

Lee, M., Park, M.S., Cheong, H.K., 2020. An association between oil spill clean-up work and cardiovascular disease. Ecotoxicol. Environ. Saf. 194, 110284. https://doi.org/10.1016/j.ecoenv.2020.110284 [published Online First: 2020/03/08].

Mannucci, P.M., Harari, S., Franchini, M., 2019. Novel evidence for a greater burden of ambient air pollution on cardiovascular disease. Haematologica 104 (12), 2349–2357. https://doi.org/10.3324/haematol.2019.225086 [published Online First: 2019/11/02].

Marris, C.R., Kompella, S.N., Miller, M.R., et al., 2020. Polyaromatic hydrocarbons in pollution: a heart-breaking matter. J. Physiol. 598 (2), 227–247. https://doi.org/10.1113/JP278885 [published Online First: 2019/12/17].

McNutt, M.K., Camilli, R., Crone, T.J., et al., 2012. Review of flow rate estimates of the Deepwater Horizon oil spill. Proc. Natl. Acad. Sci. U S A 109 (50), 20260–20267. https://doi.org/10.1073/pnas.1112139108 [published Online First: 2011/12/22].

Meo, S.-A.-A.-D.-A., Meo, I.M., Al-Saadi, M.M., Azeem, M.A., 2008. Lung function in subjects exposed to crude oil spill into sea water. Mar. Pollut. Bull. 56, 88–94.

Meo, S.-A.-A.-D.-A., Rasheed, S., Meo, I.M., Al-Saadi, M.M., Ghani, H.A., Alkandari, J.R., 2009. Health complaints among subjects involved in oil cleanup operations during oil spillage from a Greek tanker "Tasman Spirit". Int. J. Occup. Med. Environ. Health 22, 143–148.

Millemann, D.R., Portier, R.J., Olson, G., et al., 2015. Particulate accumulations in the vital organs of wild Brevoortia patronus from the northern Gulf of Mexico after the Deepwater Horizon oil spill. Ecotoxicology 24 (9), 1831–1847. https://doi.org/10.1007/s10646-015-1520-y [published Online First: 2015/07/26].

Na, J.U., Sim, M.S., Jo, I.J., et al., 2012. The duration of acute health problems in people involved with the cleanup operation of the Hebei Spirit oil spill. Mar. Pollut. Bull. 64 (6), 1246–1251 doi: 10.016/j.marpolbul.2012.03.013. Epub 12 Apr 9.

National Commission on the BP Deepwater Horizon Oil Spill and Offshore Drilling, 2011. Deepwater: The Gulf Oil Disaster and the Future of Offshore Drilling. Report to the President. Washington, D.C.

Nelson, D., Heuer, R.M., Cox, G.K., et al., 2016. Effects of crude oil on in situ cardiac function in young adult mahi-mahi (Coryphaena hippurus). Aquat. Toxicol. 180, 274–281. https://doi.org/10.1016/j.aquatox.2016.10.012 [published Online First: 2016/10/22].

Noh, S.R., Kim, J.A., Cheong, H.K., et al., 2019. Hebei Spirit oil spill and its long-term effect on children's asthma symptoms. Environ. Pollut. 248, 286–294. https://doi.org/10.1016/j.envpol.2019.02.034 [published Online First: 2019/02/25].

O'Donnell, F.L., Stahlman, S., Oetting, A.A., 2018. Incidence rates of diagnoses of cardiovascular diseases and associated risk factors, active component, U.S. Armed Forces, 2007-2016. MSMR 25 (3), 12–18.

O'Malley, K.J., Cook, K.F., Price, M.D., et al., 2005. Measuring diagnoses: ICD code accuracy. Health Serv. Res. 40 (5 Pt 2), 1620–1639. https://doi.org/10.1111/j.1475-6773.2005.00444.x [published Online First: 2005/09/24].

Peres, L.C., Trapido, E., Rung, A.L., et al., 2016. The Deepwater Horizon Oil Spill and Physical Health among Adult Women in Southern Louisiana: The Women and Their Children's Health (WaTCH) Study. Environ. Health Perspect. 124 (8), 1208–1213 doi: 10.89/ehp.1510348. Epub 2016 Jan 22.

Petersen, M.R., Deddens, J.A., 2009. A revised SAS macro for maximum likelihood estimation of prevalence ratios using the COPY method. Occup. Environ. Med. 66 (9), 639. https://doi.org/10.1136/oem.2008.043018 [published Online First: 2009/08/20].

Rhon, D.I., Clewley, D., Young, J.L., et al., 2018. Leveraging healthcare utilization to explore outcomes from musculoskeletal disorders: methodology for defining relevant variables from a health services data repository. BMC Med. Inf. Decis. Making 18 (1),

10. https://doi.org/10.1186/s12911-018-0588-8 [published Online First: 2018/02/02].
Roberts, J.R., Anderson, S.E., Kan, H., et al., 2014. Evaluation of Pulmonary and Systemic Toxicity of Oil Dispersant (COREXIT EC9500A((R))) Following Acute Repeated Inhalation Exposure. Environ. Health Insights 8 (Suppl 1), 63–74. https://doi.org/10.4137/EHI.S15262 [published Online First: 2014/01/01].
Rusiecki, J., Alexander, M., Schwartz, E.G., et al., 2017. The Deepwater Horizon Oil Spill Coast Guard Cohort study. Occup. Environ. Med. 12 (104343), 2017–104343.
Shane III, L., 2019. 'Deploy or get out' policy may not have forced out any troops at all. Military Times.
Shrier, I., Platt, R.W., 2008. Reducing bias through directed acyclic graphs. BMC Med. Res. Methodol. 8 (70), 1–15. https://doi.org/10.1186/1471-2288-8-70.
Strelitz, J., Engel, L.S., Kwok, R.K., et al., 2018. Deepwater Horizon oil spill exposures and nonfatal myocardial infarction in the GuLF STUDY. Environ Health 17 (1), 69. https://doi.org/10.1186/s12940-018-0408-8 [published Online First: 2018/08/27].
Strelitz, J., Sandler, D.P., Keil, A.P., et al., 2019. Exposure to Total Hydrocarbons During Cleanup of the Deepwater Horizon Oil Spill and Risk of Heart Attack Across 5 Years of Follow-up. Am. J. Epidemiol. 188 (5), 917–927. https://doi.org/10.1093/aje/kwz017 [published Online First: 2019/01/31].
Strelitz, J., Keil, A.P., Richardson, D.B., et al., 2019. Self-reported myocardial infarction and fatal coronary heart disease among oil spill workers and community members 5 years after Deepwater Horizon. Environ. Res. 168, 70–79. https://doi.org/10.1016/j.envres.2018.09.026 [published Online First: 2018/10/03].
Suarez, B.L.V., Perez-Gomez, B., Aragones, N., Rodriguez-Artalejo, F., Marques, F., et al., 2005. Acute health problems among subjects involved in the cleanup operation following the Prestige oil spill in Asturias and Cantabria (Spain). Environ. Res. 99, 413–424.
Temkin, A.M., Bowers, R.R., Magaletta, M.E., et al., 2016. Effects of Crude Oil/Dispersant Mixture and Dispersant Components on PPARgamma Activity in Vitro and in Vivo: Identification of Dioctyl Sodium Sulfosuccinate (DOSS; CAS #577-11-7) as a Probable Obesogen. Environ. Health Perspect. 124 (1), 112–119. https://doi.org/10.1289/ehp.1409672 [published Online First: 2015/07/03].
U.S. Coast Guard, 2018. Coast Guard Occupational Medicine Manual: Department of Homeland Security.
Zock, J.-P.-R.-T.-G., Pozo-Rodriguez, F., Barbera, J.A., Bouso, L., Torralba, Y., Anto, J.M., Gomez, F.P., Fuster, C., Verea, H., 2007. Prolonged respiratory symptoms in clean-up workers of the prestige oil spill. Am. J. Respir. Crit. Care Med. 176, 610–616.
Zock, J.P., Rodriguez-Trigo, G., Rodriguez-Rodriguez, E., et al., 2014. Evaluation of the persistence of functional and biological respiratory health effects in clean-up workers 6 years after the prestige oil spill. Environ. Int. 62, 72–77. https://doi.org/10.1016/j.envint.2013.09.020. Epub 13 Oct 26.